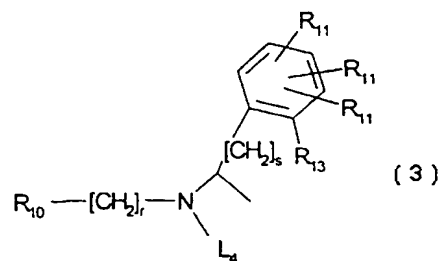
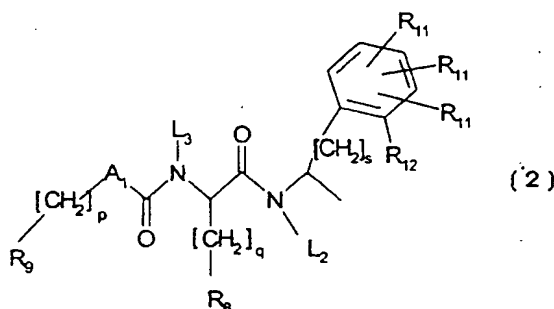
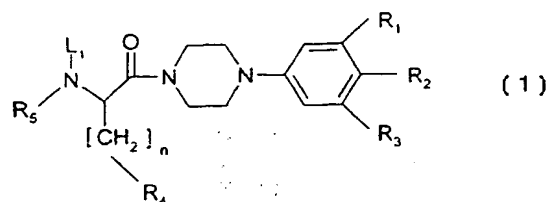


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(21) International Application Number: PCT/GB99/02957 (22) International Filing Date: 7 September 1999 (07.09.99) (30) Priority Data: 9819860.9 12 September 1998 (12.09.98) GB (71) Applicant (for all designated States except US): ZENECA LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): LUKE, Richard, William, Arthur [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). JEWSBURY, Philip, John [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). COTTON, Ronald [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). (74) Agent: BRYANT, Tracey; AstraZeneca PLC, Global Intel- lectual Property, Alderley Park, Mereside, Macclesfield, Cheshire SK10 4TG (GB).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: PIPERIZINE-4-PHENYL DERIVATIVES AS INHIBITORS OF THE INTERACTION BETWEEN MDM2 AND 53



(57) Abstract

A compound of formula (1), wherein: R₅ is hydrogen, C₁₋₄alkyl, R₆CH₂- or R₆C(O)-; R₆ is aryl, heteroaryl, heterocyclyl, aminoC₃₋₆alkyl, N-(C₁₋₄alkyl)aminoC₃₋₆alkyl, NN-(diC₁₋₄alkyl)aminoC₃₋₆alkyl, or R₇; wherein the aryl, heteroaryl or heterocyclyl rings may be optionally substituted with up to three substituents independently selected from nitro, C₁₋₄alkyl, C₁₋₄alkoxy, halo, (C₁₋₄alkyl)sulfanyl, C₁₋₄alkoxycarbonyl, N-(C₁₋₄alkyl)carbamoyl, NN-(diC₁₋₄alkyl)carbamoyl, N-(C₁₋₄alkyl)amino or NN-(diC₁₋₄alkyl)amino; wherein R₇ is either a group or formula (2) or formula (3); and wherein L₁, L₂, L₃, L₄, R₁, R₂, R₃, R₄, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄, R₂₅, R₂₆, R₂₇, R₂₈, R₂₉, R₃₀, R₃₁, R₃₂, R₃₃, R₃₄, R₃₅, R₃₆, R₃₇, R₃₈, R₃₉, R₄₀, R₄₁, R₄₂, R₄₃, R₄₄, R₄₅, R₄₆, R₄₇, R₄₈, R₄₉, R₅₀, R₅₁, R₅₂, R₅₃, R₅₄, R₅₅, R₅₆, R₅₇, R₅₈, R₅₉, R₆₀, R₆₁, R₆₂, R₆₃, R₆₄, R₆₅, R₆₆, R₆₇, R₆₈, R₆₉, R₇₀, R₇₁, R₇₂, R₇₃, R₇₄, R₇₅, R₇₆, R₇₇, R₇₈, R₇₉, R₈₀, R₈₁, R₈₂, R₈₃, R₈₄, R₈₅, R₈₆, R₈₇, R₈₈, R₈₉, R₉₀, R₉₁, R₉₂, R₉₃, R₉₄, R₉₅, R₉₆, R₉₇, R₉₈, R₉₉, R₁₀₀ are as defined in claim 1. The compounds of formula (1) inhibit the interactions between MDM2 and p53 and may be useful in the treatment of cancers.